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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,765	02/12/2007	Long Dang	001107.00591	6733

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EXAMINER	
WARE, DEBORAH K	

ART UNIT	PAPER NUMBER
1651	

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07/06/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,765	DANG ET AL.	
	Examiner	Art Unit	
	DEBBIE K. WARE	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply with Sequence disclosures*.

DETAILED ACTION

Claims 1-24 are presented for reconsideration on the merits.

37 CFR 1.821-1.825

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure set forth in 37 CFR 1.821-1.825 for the reasons set forth on Notice to Comply with Sequence Disclosures. Applicants are requested to review the specification and complete disclosure carefully to make sure that they are in full compliance with these rules as indicated in the Notice (e.g. note page 12, of the specification but others may be disclosed which do not comply either not indicated on page 12, the Examiner did not find other places wherein sequences are disclosed but there may be other occurrences which Applicants might take note of upon further review).

Brief Description of the Drawings

The Brief Description of the Drawings in the specification is objected to under 37 CFR 1.74 and in accordance with MPEP 608.01(f). Figure 4 in the Brief Description of the Drawings does not adequately describe Fig A-Fig D; nor does Figure 10 in Brief Description describe Fig 10A-Fig 10F. Therefore, the Brief Description is objected to and Applicants are required to provide a brief description of these drawings in accordance with MPEP 608.01(f).

Response to Amendment

The amendment filed March 26, 2010, has been received and entered.

Response to Arguments

Applicants' arguments have been deemed persuasive with respect to the previous rejections of record and hence these rejections under 35 USC 102 have been removed. However, in light of these arguments and upon an updated search of the claims new art has been discovered. Furthermore, other issues have come to the attention of the Examiner which are set forth as follows.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-24 recite a bacterium which is "toxin defective" or a bacterium in which all or part of "a toxin gene of a wild type form" of the anaerobic bacterium is deleted.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus,

and because the genus is highly variant, "toxin defective/toxin deleted" alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Note that there are no examples showing the efficacy of using C. sordellii, nor has a strain been created as a representative of this species. Thus, applicants were not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."

Applicant is reminded that Vas-Cath make clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Furthermore, in The Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every

species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating tumors with Clostridium novyi-NT strain, by deleting the lethal toxin gene on the phage episome, does not reasonably provide enablement for methods of treating tumors with any anaerobic bacterium, or any strain of C. novyi or C. sordellii, having a toxin gene deleted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Applicants' specification provides no disclosure of how to obtain them nor do any of the examples of the specification use any other strain than C. novyi-NT strain.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the

invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731,737, 8 USPQ2d1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir 1999).

Dang et al (reference cited on enclosed PTO-892 Form) sets forth that sequential treatment of C. novyi-NT spores, dolastatin-10 and MMC, resulted in dramatic effects on large tumors. However, Dang et al further set forth that results were "rarely" seen with C. novyi NT alone. (See page 5). Accordingly, one of skill in the art would be forced into excessive experimentation to identify a particular anaerobic bacterium having a toxin gene deleted, which can regress, slow or arrest the growth of a tumor.

Given the lack of guidance, lack of working examples, and the unpredictable nature of the invention, one of skill in the art would be forced into excessive experimentation in order to practice the instantly claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Since the microorganism is recited in the claims, it is essential to the invention recited in those claims. It must therefore be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism is not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the microorganism is readily available to the public. The exemplified disclosure requires the use of the created strain C. novyi-NT and no other strains have been identified per se. Also, C. novyi-NT strain nor any other strain have been deposited. Applicants' disclosure does not provide a repeatable process for obtaining the strain C. novyi-NT, and all of the examples require this strain for carrying out the claimed invention. With the lack of guidance in the specification for obtaining the exemplified strain or any other strain having the characteristics as required in the claims and an assurance of its availability to the public upon the issuance of a patent in this case if one should issue, the microorganism may be deposited by Applicants.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over previously cited Dang et al (USP 7344710) in view of **newly cited** Tito Fojo & Paraskevi Giannakakou (Fojo et al), cited on previously enclosed PTO-1449 Form, and **newly cited** Helson et al (USP 5688517), **newly cited** Dewhirst et al (USP 5554638), US patents (USP) cited on enclosed PTO-892 Form.

Claims are drawn to method for treating tumors in a mammal and kit therefore. The method comprises administering to the mammal spores of a toxin-defective, anaerobic bacterium and administering to the mammal a microtubule stabilizing anti-tumor agent; whereby the tumor regresses or its growth is slowed or arrested. The kit

for treating tumors has components that are in a divided or undivided container wherein the components are the spores of the bacterium, as required by the method, and stabilizing agent as required by the method. The bacterium is Clostridium novyi or Clostridium sordellii. The kit further comprises a nitric oxide synthetase (NOS) Inhibitor, and the agent can be taxol, taxotere, cephalomannine, epothilone B or taxane. The method requires administering steps which is performed serially and can be done intravenously, intratumorally

Dang et al. teach method and kit, therefore, for treating tumors in a mammal, comprising administering to the mammal spores of a toxin-defective, bacterium (anaerobic) and administering an anti-tumor agent to slow the tumor growth. Note col. 2, lines 1-25 and col. 4, lines 35-67, also see the entire abstract.

Fojo et al teach microtuble stabilizing agents to include taxane (p. 296, col. 1, lines 1-2), taxotere (p. 297, col. 1, line 18), taxol (p. 294, col. 1, line 13), taxane (p. 294, col. 1, line 11), and epothilone B (p. 294, col. 1, lines 13-14). These agents are used as anti-tumor agents, see introduction at p. 293.

Helson et al teach use of cephalomannine for treating tumor in a mammal, see abstract.

Dewhirst et al teach NOS Inhibitor is used as antitumor therapy to reduce tumor blood flow and oxygenation, see abstract. Further, it is administered with antitumor agents to enhance effectiveness of treating a tumor in a mammal. See abstract.

Claims differ from Dang et al in that microtuble stabilizing agents not used for combination bacateriolytic therapy for the treatment of tumors in mammals or in the kit, therefore.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace the agents disclosed by Dang et al with the agents disclosed by Fojo et al, Helson et al and to further select for use in the antitumor therapy of Dang et al the inhibitor disclosed by Dehwhirst et al because each have been used in the art for enhancement of effectiveness for the treatment of tumors. Each of the claim features are disclosed in the art. One of skill would have been motivated to replace the agents of Dang et al with the agents of Fojo et al, Helson and to further select the inhibitor as disclosed by Dewhirst et al because stabilizing agents suppress microtubule dynamics without increasing in polymer mass or formation of microtubule bundles. Clearly one of skill would have known that the microtubule stabilizing agents would provide successful results. To provide for kit, therefore, comprising these key components is clearly within the purview of an ordinary artisan. The claims are, therefore, rendered *prima facie* obvious over the cited prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 20 of U.S. Patent No. 7344710 in view of Fojo et al, Helson et al and Dewhirst et al, all cited and discussed above.

The claims differ from the patented claims in that microtubule destabilizing agents are selected for use with the spores for combination bacteriolytic cancer therapy, and hence the only difference is scope per se, because the patented claims do not

necessarily require microtubule destabilizing agents as the anti-tumor agents to be combined with the spores for combination bacteriolytic cancer therapy.

The '710 claims are drawn to administering spores of an isolated strain which is toxin-defective as claimed herein and also can administer an anti-tumor agent therewith, of which administering is carried out intravenously or intratumorally. Also the spores and agent are administered serially.

Each of Fojo et al, Helson et al and Dewhirst et al are discussed above.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to select replace the antitumor agent of '710 with the agents of the cited prior art to provide for the administering of the spores and microtuble stabilizing agents. One of skill in the art would have expected successful results and furthermore, would have been motivated as discussed above, to select for microtuble stabilizing agents. The agents are well known in the art and to select any one of these agents is well within the purview of an ordinary artisan. The claims are *prima facie* obvious over the patented claims.

All claims fail to be patentably distinguishable over the state of the art discussed above and cited on the enclosed PTO-892 and/or PTO-1449. Therefore, the claims are properly rejected.

The remaining references listed on the enclosed PTO-892 and/or PTO-1449 are cited to further show the state of the art.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DEBBIE K. WARE whose telephone number is (571)272-0924. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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